Ethoprop Technical Briefing

September 2, 1999

Introduction and Background Information

Introduction

Purpose of Briefing

- Present overview of Ethoprop risk estimates
- Begin next phase of public participation (TRAC Pilot Process)
- Identify where to focus mitigation

Introduction

Ethoprop Risk Assessments Consider:

- Dietary Risk
  - Food
  - Drinking water
- Occupational Risk
  - Handlers
  - Post-application workers
- Non-Occupational Risk
  - Recreational (golfers)
- Ecological Risk
  - Birds
  - Mammals
  - Fish and other aquatic species
- Aggregate Risk
  - Dietary Risk
  - Non-occupational Risk

Introduction

TRAC Pilot Public Participation Process for Ethoprop

Phase	Health Effects Assessment	Ecological Assessment
❶ "Error Only" Review	7/98	10/98
❷ Error Correction	9/98	12/98
❸ Public Comment Period	11/98	2/99
❹ Revised Assessment to USDA	5/99	5/99
❺ Develop Risk Mgt. Options	9/2/99	9/2/99
❻ Develop Transition Strategy		

Introduction

Phase 1: "Error Only" Review

Phase 2: Error Correction

- Concerns for acute dietary risk, worker risk, and ecological risk

Introduction

Phase 3: Public Comment Period

- 60-day public comment period
- Comments received from registrant, public interest groups, growers, USDA
  - Importance to agriculture
  - Lack of alternatives for potatoes
  - Agency methodologies, assumptions, and modeling

Introduction

Phase 4: Revise Assessments, Solicit Comments from USDA

- **Revisions to acute dietary assessment:**
  - DEEM™ probabilistic acute & chronic assessment
  - USDA (1989-1992) food consumption database
  - Use of field trial data
  - Use of percent crop-treated data for all commodities
  - Use of ½ LOD to represent non-detects
- Estimations of DWLOCs

Introduction

Phase 4: Revise Assessments, Solicit Comments from USDA

- Revisions to occupational risk assessment
  - Combining dermal and inhalation risks
  - Golf course worker risk
  - Post-application worker risk
- Performed non-occupational risk assessment
  - Recreational (golfers)
- Modifications to ecological risk assessment
  - Addition of typical application rate
  - Risk conclusions did not change
  - Evaluation of data on bird kills

Introduction

Phase 4: Revise Assessments, Solicit Comments from USDA

- USDA:
  - Asked questions on science and policy issues
  - Provided information
  - Commented on the need to maintain more than one pesticide for a specific pest problem

Phase 5

- Technical Briefing
- Revised risk assessment (incorporating all studies) available in public docket and on the internet
- Begin 60-day public participation period
- Public submits risk management ideas
- Opportunities for growers and others to meet with EPA

Regulatory History

- First registered in 1967
- Registration transferred to Rhône-Poulenc in 1981
- There have been 2 Ethoprop Registration Standards issued
  - The most recent was June 1988
- Currently, 22 tolerances established
- FRN proposed revocation of 6 ethoprop tolerances

Use Profile

- Type of Pesticide
  - Insecticide
  - Nematicide
- Registered Uses
  - 11 Food Uses (>80% of use) (bananas, plantains, potatoes, sweet potatoes, sugarcane, corn (field & sweet), peanuts, cucumbers, pineapple, beans (succulent & dry), cabbage)
  - Tobacco, ornamentals, and golf course turf

Use Profile

- Method of Application
  - Ground
  - Aerial
    - Granular formulation on potatoes only
    - Registrant has offered to voluntarily cancel this use
  - Typically 1 application per season-most uses
  - Agricultural application rates range from 2 to 12 lb ai/acre

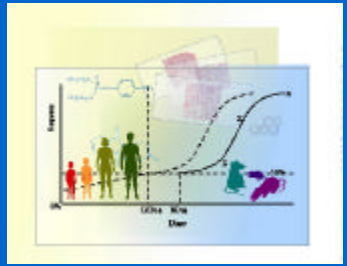
Use Profile

- Major Pests
  - Nematodes - most crops
  - Garden symphylam - beans, potatoes
  - Banana root borer - banana
  - Corn root worm - corn, peanuts
  - Cutworm - corn
  - Wireworm - potatoes, sweet potatoes, sugarcane
  - White grubs - sweet potatoes

Use Profile

- <1 million pounds a.i. used annually in U.S.
  - ~35% on potatoes (3% crop treated)
  - ~28% on sugarcane (7% crop treated - highest)
  - ~14% on tobacco (3% crop treated)
  - Other U.S. crops (4% or less crop treated)
- Mainly in Northwest and South
- Sources of Usage Data
  - USDA-NASS
  - Rhone-Poulenc
  - National Center for Food & Agricultural Policy
  - EPA

Human Health Risk Assessment



www.epa.gov/pesticides/op/ethoprop.htm

Risk Assessment Components

- Dietary
  - Food
  - Drinking Water
- Occupational
  - Handlers
  - Post-application Workers
- Non-Occupational
  - Recreational (golfers)
- Aggregate (food, drinking water, recreational)

Dietary Risk Equation

Risk = Hazard x Exposure, where

Exposure = Consumption x Residue

Effect Levels

- Lowest Observed Adverse Effect Level = LOAEL
  - Is the lowest dose at which an “adverse” health effect is seen. Has units of mg per kg body weight per day.
- No Observed Adverse Effect Level = NOAEL
  - Is the highest dose at which no “adverse” health effect is seen. This dose is less than the LOAEL. Has units of mg per kg body weight per day.

Acute Hazard (toxicity)

- **Study**: 90-day Dog Dietary Study showed plasma cholinesterase inhibition on day 2
- **Endpoint**: Plasma cholinesterase inhibition
  - **LOAEL**: 0.075 mg/kg/day
  - **NOAEL**: 0.025 mg/kg/day
- *Endpoint from this study most accurately reflects toxicity which could result from one-day dietary exposure to ethoprop*

Chronic Hazard (Toxicity)

- **Study**: 5-month and 1-year toxicity studies in dogs showed plasma cholinesterase inhibition
- **Endpoint**: Plasma cholinesterase Inhibition
  - **LOAEL**: 0.025 mg/kg/day
  - **NOAEL**: 0.01 mg/kg/day
- *Endpoint from these studies most accurately reflect toxicity which could result from long-term dietary exposure to ethoprop.*

Chronic Cancer Risk

- **Study**: 2-year Feeding Study in Rats
  - found increased adrenal pheochromocytomas in male rats
- **Cancer Classification**
  - "Likely" human carcinogen
  - regulated with a linear low-dose (Q_1*) approach
  - Q_1* = 0.0281 $(mg/kg/day)^{-1}$

Analysis of Special Sensitivity of Infants and Children

- No developmental effects in fetuses
- No toxicity to offspring below maternally toxic doses
- No increased sensitivity in pups relative to adults
- No abnormalities in developing fetal nervous system
- No histopathology of the nervous system
- Complete toxicity database
- Good data - unlikely that exposures are underestimated

Uncertainty Factors for Non-Cancer Hazard

❑ 10X	Interspecies Variability
❑ 10X	Intraspecies Sensitivity
❑ 1X	FQPA Safety Factor Removed
❑ 100X	Total UF for all Human Health Risk Assessments

Reference and Population Adjusted Doses

$$RfD = \frac{NOAEL}{UF}$$

$$PAD = \frac{RfD}{FQPA\ Safety\ Factor}$$

For ethoprop:

- FQPA Safety Factor = 1
- RfD = PAD

Population Adjusted Doses for Ethoprop

- Acute PAD = 0.00025 mg/kg/day
- Chronic PAD = 0.0001 mg/kg/day

Types of Risk Assessments

- **Acute Dietary:**

  Conducted Tier 2 (non-probabilistic) and Tier 3 (probabilistic) assessments

  - Tier 2 assumed tolerance level residues, % of crop treated, field trials, and processing data
  - Tier 3 used % of crop treated, field trials, processing data, adjustment factors
    - monitoring data available

Residue Data

- Residues on crops
  - Monitoring data
    - USDA, PDP
    - FDA, Surveillance
  - Field Trials
- Metabolism Data
  - Plants

PDP Residue Data

- Limited samples
  - <100 samples per commodity
  - Samples only available for 1-year (1994)
- PDP Data were not used
- Parent only
- No Detects
  - LOD = 0.03 ppm

FDA Residue Data

- No Detects
  - LOD = 0.015 ppm
- Parent only
- FDA Data were not used
- Many Samples
  - range 140 (corn) to 1301 (potatoes)

Field Trial Residue Data

- Parent plus metabolite M1
- Few Detects
  - beans (green and lima)
  - peanuts
- LOD = 0.003 ppm

Metabolism Studies

- Plants
  - corn
  - potatoes
  - cabbage
- Rotational crops
  - radish
  - spinach
  - wheat

Residues of Concern

- Acute & Chronic
  - Ethoprop and metabolites:
    - SME (O-ethyl-S-methyl-propylphosphorodithioate)
    - OME (O-ethyl-O-methyl-S-propylphosphorothioate)
- Cancer
  - Ethoprop and metabolites:
    - SME (O-ethyl-S-methyl-propylphosphorodithioate)
    - OME (O-ethyl-O-methyl-S-propylphosphorothioate)
    - M1 (O-ethyl-S-propylphosphorothioate)

Residue Adjustment Factors (AF)

- Derived from metabolism studies and crop rotation studies
- Used to account for total residue of concern: (Residue)(AF) = Total Residue of Concern

Residue Inputs for Dietary Risk Assessments

- Residue Data from field trials
  - ½ LOD = 0.0015 ppm
- Adjustment Factors
  - 1.1x (potatoes) to 6.0x (corn)
- % Crop treated

Acute Dietary Risk Estimated as % aPAD

Population	% aPAD (at 99.9)
U.S Population	39
Infants <1yr.	75
Children 1-6	67
Children 7-12	35

Chronic & Cancer Dietary Risk Estimated

Population	% cPAD
U.S Population	0.5
Infants <1yr.	1.0
Children 1-6	1.2
Children 7-12	0.7

Cancer Risk: 1.1×10^{-8}

Drinking Water Risk Assessment

- The available monitoring data could not be used
- The Agency generates surface and ground water estimated environmental concentrations based on:
  - Environmental fate data
  - Modeling
- The Agency assesses risks based on:
  - Toxicity of ethoprop
  - Estimated environmental concentrations

Drinking Water Risk Assessment

- Determined exposure to ethoprop in food first, then considered any remaining allowable exposure in drinking water
- Example:
  - For non-nursing infants, 1.3% of the chronic PAD used by exposure through food
  - 98.7% of the chronic PAD remaining for exposure through drinking water

Drinking Water Risk Assessment

- Drinking water exposure based on model estimates exceeded the amount of the acute and chronic PADs allocated for ground & surface water
  - Conclude: acute and chronic exposure to ethoprop in drinking water may be of concern
  - There are also concerns for cancer risk

Occupational Exposure and Risk Assessments

Handlers

- Professional pesticide applicators and individual farmers/growers who mix, load and apply pesticides; aerial flaggers
- Turf management professionals (golf courses)

Post-Application Workers

- Turf management professionals who perform tasks after pesticide application (golf courses)
- Generally no concerns for harvesters due to pre-plant/pre-emergent use

Non-Occupational Exposure & Risk Assessments

Residential

- No registered uses
- No risk assessment conducted

Recreational

- Individuals who golf following pesticide applications to golf courses

Toxicity Endpoints for Risk Assessment

Short- and Intermediate Term for Dermal and Inhalation Exposure

DERMAL	**Study**	21-day Dermal Rabbit Toxicity Study
	NOAEL	0.1 mg/kg/day (Short- & Intermediate Term) Endpoint: Plasma, RBC, & Brain ChEI
INHALATION	**Study**	90-day Dog Feeding Study (Short-Term) 5-month Dog Gavage Study (Intermediate Term)
	NOAEL	0.025 mg/kg/day (Short-Term) 0.010 mg/kg/day (Intermediate-Term) Endpoint: Plasma ChEI

Handler Assessment

Supported Ethoprop Uses:

- Four formulations
- Assessment conducted for use on 11 food crops, tobacco, ornamentals, and golf course turf
- Applied by air, backpack sprayer, chemigation, dipping, groundboom, hand, handheld measuring container, low-pressure handwand, push-type and tractor-drawn spreaders and sprinkler
- Applied at rates of 1.2 to 20 lbs ai per acre, depending on commodity

Handler Assessment

Handler Exposure and Risk Calculations

$$\text{Dose} = \frac{(\text{Unit Exposure}) \times (\text{Amount Handled}) \times (\%\ \text{Absorption})}{\text{Body Weight}}$$

$$\text{Margin Of Exposure (MOE)} = \frac{\text{NOAEL (mg/kg/day)}}{\text{Dose (mg/kg/day)}}$$

Correction for dermal absorption is not required because dermal toxicity studies used, 100% absorption assumed for inhalation route

Handler Assessment

Ethoprop Agriculture	Combined Dermal & Inhalation MOEs	
	PPE	Engineering Controls
Short-term Exposures	0.033 - 9.0	0.17 - 30
Intermediate-term Exposures	0.033 - 7.9	0.11 - 18

Handler Assessment

Ethoprop Golf Courses	Combined Dermal & Inhalation MOEs	
	PPE	Engineering Controls
Short-term Exposures	0.1 – 1.9	2.9 – 5.5
Intermediate-term Exposures	0.1 – 1.6	2.0 – 3.3

Cancer Risk Assessment

Ethoprop Agriculture	Combined Dermal & Inhalation Risk	
	PPE	Engineering Controls
Individual	3.6E-7 - 7.9E-4	8.1E-8 - 8.4E-5
Professional	3.9E-6 - 2.3E-3	8.1E-7 - 8.4E-4

Cancer Risk Assessment

Ethoprop Golf Courses	Combined Dermal & Inhalation Risk	
	PPE	Engineering Controls
Individual	3.9E-6 - 7.9E-5	9.0E-7 - 2.0E-6
Professional	3.9E-5 - 7.9E-4	9.0E-6 - 2.0E-5

Handler Risk Assessment Summary

- No chemical-specific data available, so PHED data were used
- Combined dermal & inhalation risks were calculated based on the maximum PPE and/or engineering controls
- Risks are of concern for all scenarios (both agricultural and turf management), regardless of the use of engineering controls and personal protective clothing

Handler Cancer Risk Assessment Summary

- Combined dermal & inhalation risks were calculated based on the maximum PPE and/or engineering controls
- Risks are of concern for one individual scenario and five professional pesticide applicator scenarios which yielded cancer risks greater than 1×10^{-4}

Post-Application Worker Assessment

Turf Management Professionals' Dermal Risk Results

Task	Days After Treatment	MOE	Cancer Risk
Tractor			4.9 E-5
Mowing after 20 lbs ai/A	62	107	
Mowing after 10 lbs ai/A	55	103	
Push-type Mower			9.9 E-5
Mowing after 20 lbs ai/A	68	101	
Mowing after 10 lbs ai/A	62	107	

Agricultural

- generally no concerns due to the use patterns (i.e., pre-plant/pre-emergent, soil incorporation)

Non-Occupational/Recreational Assessment

Adult Golfer Dermal Risk Results

Task	Days After Treatment	MOE	Cancer Risk
20 lbs ai/A			1.8 E-6 - 3.5 E-6
	0	2	
	40	106	
10 lbs ai/A			1.2 E-6 - 5.1 E-6
	0	3	
	33	101	

Ethoprop Incident Reports

Poison Control Centers (1985-1996)

- 40 occupational incidents reported
- 47 non-occupational incidents reported (bystanders)
- Above average evidence of risk (e.g., hospitalization) compared to other OPs and carbamates
- Too few cases for detailed analysis

Aggregate Risk Assessment

- Combines exposures from:
  - Food
  - Drinking water
  - Recreational (golfers)
- Both adults and children considered

Aggregate Risk Assessment - Results

Acute & Chronic Aggregate

- Food & Water Only
- Food Exposure Not of Concern
- Drinking Water Exposure Based on Model May Be of Concern
- Monitoring data may refine the risks

Aggregate Risk Assessment - Results

- Short-term (Food, Water & Recreational)
  - Not combined because recreational uses alone exceeded a level of concern

Ecological Risk Assessment

Environmental Fate and Effects Assessment

- Environmental Fate Assessment
  - Laboratory and Field Studies
- Water Resource Assessment
  - Modeling and Monitoring
- Ecotoxicity
  - Acute and chronic studies
  - Birds, mammals, insects, fish, aquatic invertebrates, and plants
- Ecological Risk Assessment
  - Exposure and Toxicity
  - Incidents

Environmental Fate of Ethoprop

- Laboratory studies have shown ethoprop to be fairly persistent
  - primary route of dissipation: soil metabolism half-life of 100 days
  - In the field, dissipation can be more rapid, depending upon soil temperature and moisture, with dissipation being more rapid under warm moist conditions
  - field half-lives of 9-40 days

Environmental Fate of Ethoprop

- Based on mobility data, ethoprop can be expected to leach
- However, field studies as well as monitoring data suggest that ethoprop should not pose a significant ground water contamination problem
- Because of its high solubility and low soil binding potential, ethoprop can contaminate surface water. There have been detections of ethoprop by NAWQA.
- Since ethoprop is generally soil incorporated, then run-off potential is reduced

Drinking Water and Aquatic Assessment of Ethoprop

- Estimated environmental concentrations (EECs) generated from SCI-GROW and PRZM-EXAMS were used for a screening drinking water assessment.
- The available monitoring data are not sufficiently reliable and/or of adequate quantity for use in a quantitative drinking water assessment

Drinking Water and Aquatic Modeling

- Major crops modeled at use sites with highest EEC potential
- Highest exposures correlated with precipitation
- Total depth of incorporation key to reducing aquatic exposures

Monitoring Data

- Little monitoring targeted at major use areas
- Sample timing poorly correlated with use periods
- Crop regions of greatest concern had the least or no monitoring

Summary of Ecological Risk Assessment

- The assessment indicates that virtually all uses at all maximum labeled rates result in high risks to all terrestrial and aquatic organisms
- Risks were also estimated using lower than maximum labeled application rates however, risks were still of concern even at these lower rates
- Even though ethoprop is generally either soil incorporated or watered-in, thus reducing potential exposure, it is so highly toxic that very small amounts may kill sensitive species

Ecological Risk Assessment: Toxicity & Exposure

- Risk Quotients (RQ)
  - Ratio of exposure concentration to toxicity endpoint (non-granular products)
  - Acute RQ = $\frac{\text{Peak Environmental Concentration}}{LC_{50} \text{ or } EC_{50}}$

    Chronic RQ = $\frac{\text{Peak Environmental Concentration}}{\text{NOAEC}}$
  - For granular products, an LD_{50}/sq.ft. is calculated to assess risk
- Ratio is compared to the Agency's Levels of Concern (LOC)

Summary of Acute Toxicity

- A cholinesterase inhibitor in avian and mammalian species
- Very highly toxic to birds, aquatic invertebrates, and estuarine and marine fish
- Highly toxic to mammals and freshwater fish
- Moderately toxic to bees

Summary of Chronic Effects

- Ethoprop causes reproductive effects in birds and mammals
  - Bobwhite quail
    - reductions in viable and live embryos, % viable eggs from total eggs laid, and female body weights
  - Mallard duck
    - reductions in eggs laid, % viable eggs from total eggs laid, viable and live 3 week embryos, normal hatchlings, 14 day survivors
  - Mammals
    - decreased body weights and mortality in the offspring
- Larval fish growth is affected at low concentrations, while growth is reduced in freshwater invertebrates and survival reduced in estuarine invertebrates

Risk Characterization

- Confirmed incidents involving fish and bird kills have been reported
- Fish kills were associated primarily with golf course use
- Probably due to greater rainfall, aquatic EECs are higher in the coastal regions. Significant since majority of ethoprop use is in Florida and estuarine organisms are more sensitive to ethoprop than freshwater organisms
- It is not unreasonable to assume that fish kills are also occurring in estuarine regions; however they are more difficult to document in these areas than in inland locations

Summary of Remaining Concerns

Phase 5

- Technical Briefing
- Revised risk assessment (incorporating all studies) available in public docket and on the internet
- Begin 60-day public participation period
- Public submits risk management ideas
- Opportunities for growers and others to meet with EPA

Dietary Risk

- Food only
  - Not of concern
- Food + Water
  - May be of concern

Non-Occupational/Aggregate Risk

- Non-Occupational (Recreational) Risk
  - Risks to golfers of concern
- Aggregate Risk
  - Of concern

Occupational Risk

- Handlers
  - Of concern
- Post-application (agricultural)
  - Generally used pre-plant/pre-emergent
- Post-application (golf courses)
  - Of concern

Challenges to Refining Occupational Risk

- Highly toxic by all routes of exposure
- Based on PHED
  - No chemical-specific data available
- Dermal exposure is the significant risk driver
- Use of PPE and engineering controls were considered when feasible

Challenges To Refining Ecological Risk

- High water solubility
- Resistance to hydrolytic, photolytic and metabolic degradation in water and soil
- Very high toxicity
- Applied in the spring
- Birds and small mammals exposed during foraging

Considerations For Next Steps

- Generally, applied by ground application methods and is either watered-in or soil-incorporated
- Generally, one application per season (exceptions are pineapple and golf course turf)
- Risk quotients exceeded LOCs for most use patterns even at the lower labeled application rate of 1 lb. ai/acre
- Occupational MOEs range from less than 1 to 30

Conclusions